Adverse Reaction to Cetuximab, an Epidermal Growth Factor Receptor Inhibitor

Dear Editor,

Inhibition of the epidermal growth factor receptor (EGFR) is a new strategy in treatment of a variety of solid tumors, such as colorectal carcinoma, non-small cell lung cancer, squamous cell carcinoma of the head and neck, and pancreatic cancer (1). Cetuximab is a chimeric human-murine monoclonal antibody against EGFR. Cutaneous side effects are the most common adverse reactions occurring during epidermal growth factor receptor inhibitors (EGFRI) therapy. Papulopustular rash (acne like rash) develop with 80-86% patients receiving cetuximab, while xerosis, eczema, fissures, teleangiectasiae, hyperpigmentations, and nail and hair changes occur less frequently (2). The mechanism underlying these skin changes has not been established and understood. It seems EGFRI alter cell growth and differentiation, leading to impaired stratum corneum and cell apoptosis (3-5).

An abdominoperineal resection of the rectal adenocarcinoma (Dukes C) was performed on a 43-year-old female patient. Following surgery, adjuvant chemo-radiotherapy was applied. After two years, the patient suffered a metastatic relapse. Abdominal lymphadenopathy was detected on multi-slice computer tomography (MSCT) images, with an increased value of the carcinoembryonic antigen (CEA) tumor marker (maximal value 57 ng/mL). Hematological and biochemical tests were within normal limits, so first-line chemotherapy with oxaliplatin and a 5-fluorouracil (FOLFOX4) protocol was introduced. A wild type of the KRAS gene was confirmed in tumor tissue (diagnostic prerequisite for the introduction of EGFRI) and cetuximab (250 mg per m^2 of body surface) was added to the treatment protocol. The patient responded well to the treatment with confirmed partial regression of the tumor formations.

Three months after the patient started using cetuximab, an anti-EGFR monoclonal antibody, the patient presented with a papulopustular eruption in the seborrhoeic areas (Figure 1) and eczematoid reactions on the extremities with dry, scaly, itchy skin (Figure 2). Furthermore, hair and nail changes gradually developed, culminating with trichomegaly (Figure 3) and paronychia (Figure 4). The patient was treated with oral antibiotics (tetracycline) and a combination of topical steroids with moisturizing emollients due to xerosis, without reduction of EGFRI therapy and with a very good response. Trichomegaly was regularly sniped with scissors. Nail fungal infection was ruled out by native examination and cultivation, so antiseptics and corticosteroid ointments were introduced for paronychia treatment.

Figure 1. Papulopustular rash.

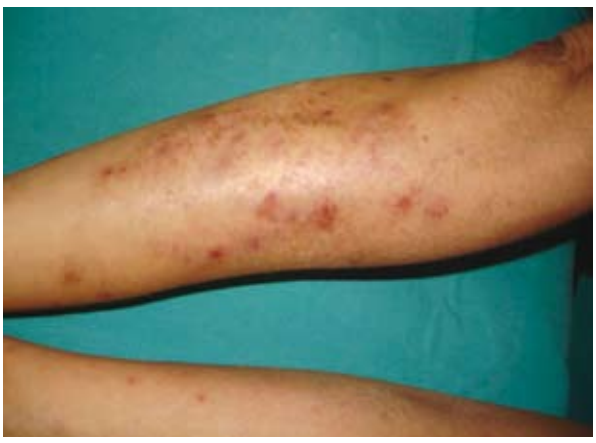

Figure 2. Xerosis of the skin.

Figure 3. Trichomegaly.

Figure 4. Paronychia.

During the above-mentioned therapy, apart from skin manifestations, iatrogenic neutropenia grade IV occurred, with one febrile episode, and because of this, the dose of cytostatic drugs was reduced. After 10 months of therapy, progression of the disease occurred with lung metastases, so EGFRI therapy was discontinued and the patient was given second-line chemotherapy for metastatic colorectal carcinoma. This led to gradual resolution of all aforementioned cutaneous manifestations.

Since the pathogenesis of skin side-effects due to EGFRI is not yet fully understood, there are no strict therapy protocols. Therapy is mainly based on clinical experience and follows the standard treatments for acne, rosacea, xerosis, paronychia, and effluvium. The therapeutic approach for papulopustular exanthema includes topical and systemic antibiotics for their antimicrobial as well as anti-inflammatory effect, sometimes in combination with topical steroids. Topical application of urea cream with K1 vitamin yielded positive results in skin-changes prevention during EGFRI therapy, especially with xerosis, eczema, and pruritus (6). Hair alterations in the form of effluvium are usually tolerable, and if needed a 2% minoxidil solution may be applied. Trichomegaly or abnormal eyelash growth can lead to serious complications, so ophthalmologic examination is needed. At the beginning of the growth, regular lash clipping may reduce possibility of corneal abrasion (7,8). Nail changes can just be a cosmetic problem (pigmentary changes, brittle nails), and in the occurrence of paronychia or onycholysis (of several or all nails) they result in high morbidity and impair daily activities. Nail management should be started as soon as possible because of slow nail growth and the relatively long half-life of EGFRI. Combination of topical iodide, corticosteroids, antibiotics, and antifungals with avoidance of nail traumatization will yield the best results (9).

EGFRI are potentially life prolonging therapies, and our goal as dermatovenereologists is to provide optimal patient care and improve their quality of life in a multidisciplinary collaboration with oncologists, radiotherapists, and ophthalmologists.

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